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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/051,253	01/18/2002	Robert L. Stout	32265	7968

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EXAMINER	
HORNING, MICHELLE S	
ART UNIT	**PAPER NUMBER**
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/051,253	STOUT, ROBERT L.	
	Examiner	Art Unit	
	Michelle Horning	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3,4,8-12,15-19,21-25 and 31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3, 4, 8-12, 15-19, 21-25 and 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This office action is responsive to communication filed 10/02/2007. The status of the claims is as follows: claims 3, 4, 8-12, 15-19, 21-25 and 31 are under current examination.

The following rejections have been withdrawn due to the persuasive affidavit and arguments by Applicants:

1. 35 USC 112, 1st paragraph (Enablement); and

2. 35 USC 112, 1st paragraph (Written Description).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 3, 4, 8-12, 15-19, 21-25 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fong et al (1996) and Fabrizi et al (1996). The limitations of the rejected claims above are as follows:

31. A method of predicting whether or not an individual has chronic HCV infection comprising the steps of obtaining a fluid sample from the individual; performing an antibody-based assay on said sample, said assay including contacting said sample with a plurality of different HCV antigens reactive with different antibodies and detecting interactions between the antigens and antibodies from the sample; determining the optical density of said sample after said antibody-based assay is performed and with said plurality of different HCV antigens present in said sample; and using the optical density to predict whether the individual has chronic HCV infection by comparing the determined optical density with a correlation curve based on the optical densities of fluid samples in combination with HCV antigen from an HCV antibody-based assay from individuals having chronic HCV infection and individuals that have cleared the HCV infection but still test positive for HCV antibodies; said method permitting a prediction having at least

ma 80% probability that the individual providing said fluid sample has chronic HCV infection. 3. The method of claim 31, said performing step including the step of contacting said sample with a quantity of HCV antigen. 4. The method of claim 31, said performance of said antibody-based assay providing results indicating whether said sample is antibody positive or antibody negative. 8. The method of claim 31, said prediction having at least a 90% probability that the individual providing said fluid sample has chronic HCV infection. 9. The method of claim 31, said prediction having at least a 95% probability that the individual providing said fluid sample has chronic HCV infection. 10. The method of claim 31, said prediction having at least a 97% probability that the individual providing said fluid sample has chronic HCV infection. 11. The method of claim 31, said method permitting a prediction that the individual has a probability of less than 50% of having chronic HCV infection. 12. A method of predicting whether an individual providing a first fluid sample comprising biological fluid testing positive for HCV antibodies from an HCV antibody assay capable of detecting more than one HCV antibody has chronic HCV infection and said assay having a plurality of different HCV antigens reactive with different antibodies therein, said method comprising the steps of: measuring the optical density of a second fluid sample, said second fluid sample comprising (I) a portion of the first fluid sample prior to conducting said the HCV antibody assay, and (ii) said plurality of different antigens from said HCV antibody assay correlating said measured optical density with a predetermined standard optical density value derived from individuals known to have chronic HCV infection; and predicting that the individual providing the first fluid sample has chronic HCV infection based on said correlation, said predicting step including the step of comparing said measured optical density with optical density ranges corresponding to certain probabilities that the individual has chronic HCV infection, said optical density ranges providing at least 80% accuracy levels for any measured optical density level. 15. The method of claim 12, said certain probability that the individual has chronic HCV infection being less than about 10% when said measured optical density is less than 1.0 in comparison to a negative control which must have an optical density of 0.1 or less at 660 nm. 16. The method of claim 12, said certain probability that the individual has chronic HCV infection being less than about 15% when said measured optical density is less than 2.35 in comparison to a negative control which must have an optical density of 0.1 or less at 660 nm. 17. The method of claim 12, said certain probability that the individual has chronic HCV infection being greater than about 70% when said measured optical density is greater than about 2.35 in comparison to a negative control which must have an optical density of 0.1 or less at 660 nm. 18. The method of claim 12, said certain probability that the individual has chronic HCV infection being greater than about 80% when said measured optical density is greater than 3.0 in comparison to a negative control which must have an optical density of 0.1 or less at 660 nm. 19. A method of predicting that an individual testing positive for HCV infection using an antibody-based assay capable of detecting more than one HCV antibody is chronically infected with HCV, said method comprising the steps of: obtaining a fluid sample from the individual; contacting said fluid sample with a plurality of different HCV antigens reactive with different antibodies to form a solution; determining the optical density of said solution having said plurality of different antigens therein; and comparing said determined optical density with a set of standard optical density values correlated with probabilities of chronic HCV infection and predicting whether or not the individual has chronic HCV based on said comparison, said comparing step including the step of using said standard optical density values to provide the probability that said individual has chronic HCV infection. 21. The method of claim t9, said probability increasing as said determined optical density increases. 22. The method of claim 19, said probability being less than 20% when said determined optical density is less than about 1.0 in comparison to a negative control which must have an optical density of 0.1 or less at 660 nm. 23. The method of claim 19, said probability being less than 20% when said determined optical density is less than about 2.35 in comparison to a negative control which must have an optical density of 0.1 or less at 660 nm. 24. The method of claim 19, said probability being greater than 70% when said determined optical density is more than about 2.35 in comparison to a negative control which must have an optical density of 0.1 or less at 660 nm. 25. The method of claim 19, said probability being greater than about 80% when said determined optical density is more than about 3.0 in comparison to a negative control which must have an optical density of 0.1 or less at 660 nm.

Fong et al discloses the clinical significance of HCV RNA status and its correlation to antibodies to structural HCV antigens (see whole document). Extensive serologic testing was performed in patients with confirmed anti-HCV reactivity to compare antibody profiles of patients with ongoing infection to those patients without detectable HCV RNA (see Introduction and Subjects and Methods). The study used two separate assays, including the RIBA 2.0 and ELISA 2.0, to determine a correlation between HCV RNA status and the pattern of antibody reactivity (see page 256). Of note, both immunoblot assays detect antibodies reactive with multiple antigens (see page 254, Methods). Figure 1b demonstrates the mean antibody titers to HCV antigen in HCV RNA positive and negative patients. This reference discloses multiple concordances in HCV-infected patients. Of relevance, the mean anti-E2 titer was significantly lower in HCV RNA negative patients and donors or nonviremic patients as revealed by ELISA testing (see page 256-7). Also, patients with undetectable HCV RNA in the serum probably have had spontaneous resolution of their HCV infection (see Abstract). This reference concludes that anti-E2 titer appears to be a useful marker of ongoing viral replication (see Discussion). While this reference characterizes HCV RNA (present or absent) to HCV antibodies correlations in viremic and nonviremic patients, this reference does not disclose the use of measuring optical density values.

Fabrizi et al evaluate the prevalence and significance of anti-HCV IgM core anitbody with anti-HCV IgG activity in the serum (see Introduction). All patients of the study were positive for anti-HCV IgG antibodies using the ELISA test while 45 were HCV RNA positive and 33 were HCV RNA negative as determined by RT-PCR (see

pages 315-6, Results). This study revealed "a statistical significance difference between HCV RNA positive and negative patients concerning the presence of anti-HCV IgM antibodies" (see page 316, Results). Most (88%) anti-HCV IgM positive patients revealed HCV RNA positivity by RT-RNA (see page 316). This reference reveals a significant association between optical density values of anti-HCV IgM and NS3, NS5 and core reactivity. Also, there was a significant relationship between optical density values and anti-HCV IgM and the number of RIBA-2 and RIBA-3 bands (page 316). Fabrizi et al disclose a positive association between frequency of anti-HCV IgM core antibody and prevalence of detectable HCV RNA in the serum (see Discussion). They also teach that the number of reactive bands in RIBA assays was significantly associated with absorbance values of anti-HCV IgM (see Discussion). Lastly, Fabrizi et al make the following recitation: "Positivity for anti-HCV IgM test kit strongly suggests detectable HCV RNA in the serum" (see Discussion, page 316).

It would have been obvious to one of ordinary skill in the art to combine the teachings of Fong et al and Fabrizi et al in order to measure the optical densities of samples in ascertaining the prevalence of HCV RNA in the serum. As discussed above, the prevalence of HCV RNA would allow one to predict whether a patient has cleared the HCV or has chronic HCV. One would have been motivated to combine the teachings given that the correlation between IgM antibodies in high concentrations to the presence of HCV RNA in serum is well characterized by Fabrizi et al. Fabrizi et al utilizes the anti-HCV IgM core assay as a serological marker to indicate the presence of ongoing HCV infection (see page 317). Additionally, Fong et al disclose that anti-E2 titer

was significantly lower in HCV RNA negative patients and that undetectable HCV RNA suggests that the patient has cleared the virus. Note that the probability of success is determined by (in part) the number of patients submitted to testing; changes in the number will lead to changes in the probability of success. There would have been a reasonable expectation of success given that such correlations are well taught in the prior art and the underlying techniques are widely used and commonly taught. Thus, the invention as whole was clearly *prima facie* obvious to the ordinary artisan at the time the invention was made.

Conclusion

NO claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michelle Horning whose telephone number is 571-272-9036. The examiner can normally be reached on Monday-Friday 8:00-5:00 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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